



## **DERIVE – Development of Riboflavin biomarkers to relate dietary sources with status, gene-nutrient Interactions and Validated health Effects in adult cohorts – & VALID – Valerolactones and healthy Ageing: Linking Dietary factors, nutrient biomarkers, metabolic status and inflammation with cognition in older adults**

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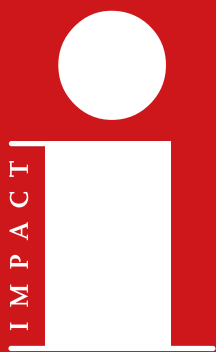
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# NOURISHING NUTRITION AND HEALTH RESEARCH



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# Understanding the benefits of riboflavin

*Professor Mary Ward introduces the DERiVE project, which is developing accessible riboflavin biomarkers for use in population studies globally, in order to investigate and address the functional and health consequences of sub-optimal riboflavin status*



**Could you begin by introducing yourself and your key research interests?**

I am a Professor of Nutrition and Dietetics at Ulster University in Northern Ireland with a particular interest in the role of B-vitamins in cardiovascular disease. The interaction between B-vitamins and a common polymorphism in the gene encoding the enzyme methylenetetrahydrofolate reductase (MTHFR) has been a main research focus in recent years. Approximately 10-12 per cent of adults in the UK and Ireland carry this genetic risk factor (TT genotype in MTHFR), which affects up to one in three adults in some populations such as Mexico.

Previous work at Ulster has led to the novel discovery that the B-vitamin riboflavin appears to be an important modulator of blood pressure in individuals with this genetic predisposition for hypertension. Our current studies aim to understand the mechanisms linking this gene nutrient interaction with blood pressure.



Biomarker analysis of Riboflavin status by DERiVE investigator Dr Liadhan McAnena, Ulster

**Can you expand on the importance of riboflavin?**

Riboflavin (vitamin B2) is a water-soluble B-vitamin that forms two important co-enzymes – flavin mononucleotide (FMN) and flavin dinucleotide (FAD). Further to its well established role in health, recent novel work undertaken by our team at Ulster demonstrated that riboflavin plays a critical role in normalising blood pressure in people with the TT genotype in the gene encoding MTHFR.

**Can you explain the benefits of good riboflavin status?**

Riboflavin (in its co-factor forms FMN and FAD) is essential for oxidation-reduction reactions, so plays a critical role in numerous metabolic pathways in the body. Thus, better riboflavin status plays an important role in maintaining health throughout the lifecycle and has been associated with a decreased risk of a number of cancers and eye disorders, including age-related cataracts. A number of studies have also shown that riboflavin intervention benefits patients with specific, albeit relatively rare, metabolic disorders, although further work is required to confirm these findings. What is entirely novel however, is the work we have been leading in recent years, which shows a blood pressure lowering effect of riboflavin in adults with a common risk factor for hypertension.

The contribution of riboflavin to health is however, very much under-recognised at this time, and the evidence greatly lacking, due to the lack of accessible biomarkers to measure riboflavin status. The proposed project will address this gap by validating riboflavin biomarkers for use in the current proposal and in future nutrition research internationally.

Our Canadian partner from the University of British Columbia in Vancouver is developing accessible biomarkers for the assessment of riboflavin status. These will then be validated by measuring biomarker status in biological samples from nationally representative cohorts in Ireland and Canada, and samples from randomised controlled trials completed at Ulster. Their reliability as biomarkers of dietary intake will be determined using data from the Irish National Adult Nutrition Survey cohort led by our partners from University College Cork in Ireland.

**What do you hope to achieve in relation to patients suffering from hypertension?**

The health impact of optimising riboflavin could be considerable. For hypertensive patients identified with the TT genotype, riboflavin supplementation can offer a simple, non-drug treatment to effectively lower blood pressure. For sub-populations worldwide with this genetic risk factor, better riboflavin status (achieved through supplements or fortified foods) may prevent or delay the onset of high blood pressure. Thus, riboflavin, targeted at those with the TT genotype in MTHFR, offers a personalised treatment or preventative strategy for hypertension, one of the leading causes of mortality worldwide. High blood pressure (hypertension) has a number of adverse health consequences; in particular, it increases a person's risk of stroke substantially. Lowering blood pressure has important health benefits: each 2mmHg decrease in systolic blood pressure is associated with a 10 per cent reduction in the risk of stroke. Thus, lowering blood pressure even by small amounts can be very beneficial. ●

# Polyphenols for healthier ageing

*Via the VALID project, Professor Helene McNulty is validating novel plasma biomarkers of polyphenol-rich foods and linking them with inflammation, metabolic health and cognition in an ageing European population*



**Could you begin by introducing yourself?**

I am Director of the Nutrition

Innovation Centre for Food and Health (NICHE) and Professor of Human Nutrition and Dietetics at Ulster University, Northern Ireland. The purpose of our research is to provide greater understanding of nutrition-related health issues, to achieve impact through facilitating food and health policy, and to drive innovation activities.

**Can you expand on your work with Professor Ward?**

A particular focus of our work involves conducting randomised controlled trials and observational studies to examine health outcomes in relation to nutritional factors, in healthy volunteers through the life cycle (from pregnancy and early life, to middle and older age) and in patient groups (such as those with cardiovascular disease, osteoporosis, cognitive dysfunction and coeliac disease).

We were strategic in setting up The Centre of Excellence in Nutrition and Ageing (CENA) within NICHE at Ulster in 2010, to enhance our existing North-South of Ireland cross-border research activities in nutrition and ageing made possible through the Trinity, Ulster and Department of Agriculture (TUDA) Ageing Cohort study. This is an invaluable resource that is being further developed through the VALID project.

**What are polyphenols and why do you believe, despite the current lack of biomarker evidence, that they may be beneficial in terms of maintaining cognitive function in older age?**

Polyphenols are among the most representative bioactive compounds, mainly present in plant-based foods, particularly grapes, nuts, berries, wine, tea and coffee. Polyphenols are not included in the category of micronutrients, as they are not essential for the maintenance of vital functions. However, several epidemiological and intervention studies show beneficial associations between long term intake of polyphenols and reduced incidence of cancer, chronic diseases and neurodegenerative processes.

In collaboration with experts in polyphenol biomarker analysis from the University of Parma, Italy, and our TUDA collaborators in Trinity College Dublin, the VALID project will identify and validate plasma-valerolactones as novel biomarkers that are modulated by dietary polyphenols and associated with cognitive function in later life.

**What is the ultimate goal for both the DERiVE and VALID projects?**

The vision and goal of both the DERiVE and VALID projects is to promote scientific excellence through international collaboration across centres of excellence, which are allowing the collection and pooling of nutrition and health data in a uniform and standardised way. Furthermore, the sharing of expertise from across the participating countries allows cross-border mobility and training of researchers and will facilitate the timely dissemination and translation of our research results to inform public health practice and policy across Europe, and indeed globally. ►

## Project Insights

### FUNDING

DERiVE funding: at Ulster University – BBSRC; BB/Po28241/1; at University College Cork – Science Foundation Ireland, 16/ERA-HDHL/3357 and at The University of British Columbia by the Canadian Institutes of Health Research – OBN-150362.

VALID funding: at Ulster University – BBSRC; BB/Po28225/1; at Trinity College Dublin – Science Foundation Ireland, 16/ERA-HDHL/3361; and at University of Parma: Ministero delle Politiche Agricole Alimentari e Forestali (MIPAAF) – D.M.31967/7303/16 del 29/12/2016.

### DERiVE PROJECT INVESTIGATORS

Prof Mary Ward (PI), Prof Helene McNulty, Prof Kristina Pentieva, Prof Sean Strain, Dr Liadhan McAnena, Dr Paul Millar and Harry Jarrett (PhD researcher) – Ulster University, UK • Prof Albert Flynn, Dr Janette Walton and Laura Kehoe (PhD researcher) – University College Cork, Ireland • Dr Yvonne Lamers, Prof John Spinelli, Dr Angela Devlin and Dr Nadia Morán – University of British Columbia, Canada

### VALID PROJECT INVESTIGATORS

Prof Helene McNulty (PI), Dr Chris Gill, Prof Mary Ward, Prof Sean Strain, Prof Adrian Moore, Dr Katie Moore, Dr Kieran Westley, Ben Parameter (PhD researcher) and Bruna Pucci (PhD researcher) – Ulster University, UK • Prof Anne Molloy, Prof Conal Cunningham, Dr Eamon Laird, Dr Kevin McCarroll, Kerrie Boyd (MRes Researcher) and Brian Mullen (MRes Researcher) – Trinity College Dublin, Ireland • Prof Daniele Del Rio, Dr Donato Angelino and Dr Pedro Mena – University of Parma, Italy

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## Impact Objectives

- Gain a better understanding of the role of nutrition in health by developing and validating novel biomarkers of dietary exposure in transnational research studies
- Grow capacity, capability and sustainable transnational partnerships in nutrition and health research, led by a UK partner in collaboration with partners in Canada, Republic of Ireland and Italy
- Demonstrate the functional and metabolic effects of optimal riboflavin status on cardiovascular health (DERiVE project), and of dietary polyphenols on the ageing brain (VALID project)

# Nourishing nutrition and health research

*Two innovative projects underway at Ulster University, Northern Ireland, are inextricably linked by their shared focus on improving nutrition with implications for health across the lifespan*

Nutrition is of the utmost importance, particularly given the phenomenon of ageing populations worldwide. The lack of validated nutritional biomarkers in some cases however, is hampering the ability of researchers to investigate the roles and health benefits of certain nutrients.

Two projects underway at Ulster University, Northern Ireland, headed up by Professors Mary Ward and Helene McNulty, respectively, are:

- Development of riboflavin biomarkers to relate dietary sources with status, gene-nutrient interactions and validated health effects in adult cohorts (DERiVE).

Project partners: Ulster University (Lead Institution), University of British Columbia (Canada) and University College Cork (Ireland).

- Valerolactones and healthy ageing: Linking dietary factors, nutrient biomarkers, metabolic status and inflammation with cognition in older adults (VALID). Project partners: Ulster University (Lead Institution), Trinity College Dublin (Ireland) and University of Parma (Italy).

### DERiVE AND VALID

The two projects are closely related and share similar goals, as Ward and McNulty explain: 'By linking these projects, it is our intention to build capacity and capability in nutrition research and to extend the

international collaborations made possible through this JPI initiative.'

The DERiVE project will develop accessible riboflavin biomarkers for use in population surveys globally, and demonstrate important functional, gene-nutrient and health effects of optimal riboflavin status.

The VALID project will validate novel biomarkers of polyphenol-rich foods and link them with inflammation, metabolic health and cognition in an ageing European population.

Both projects are in their first year and will conclude at the end of 2019.

### HEALTH IMPACTS

The goal of DERiVE is to promote health and wellness in adults, with evidence that sub-optimal riboflavin status may be a much greater global health risk than is currently recognised. 'Riboflavin has an important role in one-carbon metabolism where it interacts with other relevant nutrients (folate, vitamin B12 and vitamin B6),' Ward explains. VALID will develop and evaluate novel biomarkers that reflect dietary intakes of polyphenols (abundant in foods such as tea, cocoa, grapes, nuts and berries). 'Our research will also investigate the biological mechanisms that could link dietary polyphenols with cognitive health as people age,' McNulty adds.

Indeed, both projects are concerned with health impacts on ageing populations, as the researchers explain: 'There is an urgent need to identify public health nutrition strategies aimed at promoting better health throughout the lifecycle for healthy ageing. We are committed to generating the highest quality research to support evidence-based policies to meet the nutrition and health needs of older populations globally.'

### GROWING TRANSNATIONAL LINKS

Both projects are progressing well and, looking ahead, Ward and McNulty hope to expand these research areas. 'These projects have enabled us to develop strong international collaborations in nutrition and health and we aim to not only grow our capacity, but also the capabilities of the teams. It is also intrinsic that the transnational partnerships we are developing in Canada, the Republic of Ireland and Italy, are sustainable.'

The DERiVE and VALID projects are funded under the JPI Co-funded ERA-HDHL joint call 'Biomarker for nutrition and health'. In line with the JPI's 'A healthy diet for a healthy life' vision to support quality, translational, collaborative research, the goal of both projects is to promote scientific excellence through international collaborations. Go to: [www.healthydietforhealthylife.eu/index.php/joint-actions/era-hdhl-ja](http://www.healthydietforhealthylife.eu/index.php/joint-actions/era-hdhl-ja)